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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,433	05/10/2002	Bastian Nuyen	4512 00004	4574

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EXAMINER	
WINSTON, RANDALL O	

ART UNIT	PAPER NUMBER
1655	

MAIL DATE	DELIVERY MODE
02/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/622,433	NUYEN ET AL.	
	Examiner	Art Unit	
	Randall Winston	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *9-11,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,12-28 and 31-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but pri or to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/2007 has been entered.

Examiner has acknowledged claims 9-11 and 29-30 have been withdrawn from consideration.

Claims 1-8, 12-28 and 31-52 will be examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 35 recite the limitation "the didemnin compound" There is insufficient antecedent basis for the limitation as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 12-28 and 31-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crumb et al. (US 6,030,943) in view of Arai et al. (US 4342744) and Pribish (US 6365597) for the reasons set forth in the previous Office action which are restated below.

Applicant claims a pharmaceutical composition and a kit comprising firstly of a vial of a lyophilized didemnin preparation comprised of a didemnin compound, a water-soluble material and an alkanol/water mixture and secondly of a vial of a reconstitution solution of mixed solvents and wherein the reconstitution solution of mixed solvents comprised a surfactant (i.e. nonionic), alkanol and water for injection to be administrated to a subject.

Crumb et al. teach a pharmaceutical composition may be in form of a container (i.e. a kit is a container and the container described in Crumb is a sterile ampoule) comprising firstly of a lyophilized didemnin preparation comprised of a didemnin (i.e. aplidine and dehydrodidemnn) and a water soluble material (i.e. mannitol) and water secondly a reconstitution solution comprised of a carrier such as water used for the purpose of aiding in the injectable

administration of the pharmaceutical to a subject (see, e.g. column 5 lines 66-67 and column 6 lines 12-20).

Crumb, however, does not expressly teach that the claimed active ingredient of a surfactant and/or alkanol are mixed with water within Crumb's reconstitution solution nor alkanol are mixed within a lyophilized didemnin preparation and Crumb does not expressly teach the claimed active ingredients' ranges.

Although Crumb does not expressly teach within his reference that surfactant and/or alkanol are mixed with water within Crumb's reconstitution solution, Crumb does teaches that one of ordinary skill in the art would want to utilize surfactant and/or wetting agents within its pharmaceutical formulation and/or container (see, e.g. column 6 lines 5-11). Therefore, it would have been obvious to one of ordinary skill in the art to just place the surfactant and/or wetting agents taught within Crumb's reference within Crumb's taught reconstitution solution because surfactants and/or wetting agents are well known in the art to be effective carriers to aid in the administration of an active ingredient to a subject.

Furthermore, Arai benefically teaches that the claimed alkanol (i.e. ethanol) is an effective delivery carrier to aid in the administration of an active ingredient to a subject (see, e.g. entire document including column 7 lines 9-26, tables and claims).

Moreover, Pribish benefically teaches that ethanol is also a preferred liquid carrier in injectable solutions (see, e.g. entire patent including column 6 lines 17-21).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Crumb et al.'s pharmaceutical composition and/or kit to include the active ingredient of an alkanol (i.e. ethanol) as taught by Arai and Pribish within Crumb's pharmaceutical composition and/or kit because the three combined teachings would create the claimed pharmaceutical composition and/or kit for enhanced injectable delivery of the pharmaceutical composition's active ingredients to a subject. Furthermore, the adjustment of other conventional working conditions (e.g. the substitution of one functional equivalent alkanol for another, the ranges of each active ingredient to create solubilization of the pharmaceutical composition, the substitution of one surfactant for the other and placing the reconstitution solution within a container such as a vial), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Please note that the patentability of a product does not depend upon the method of production. If the product in a product by process claim is the same as or obvious from a product of the prior art, then the claim is unpatentable even

though the prior art product was made by a different process. (see, e.g. MPEP 2113).

Please note, the intended use of the above claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting (see, e.g., MPEP 2112).

Applicant argument has been carefully considered but is not deemed persuasive. Applicant argues that Brown teaches away from the use of water-containing composition. As such, a person of ordinary skill in art would not have been led to combine Crumb, which is about administering a poorly soluble drug (aplidine) in water, with Brown, which tells one to administer poorly water soluble cytostatic agents in anhydrous compositions that contain materials, which from a solubility standpoint, would be incompatible with water.

Although Applicant argues a person of ordinary skill in art would not have been led to combine Crumb and Brown, Examiner has amended this non-final rejection to include other references such as Arai and Pribish to demonstrate that the above cited references of Crumb, Arai and Pribish as a whole would create the claimed pharmaceutical composition and/or kit for enhanced injectable delivery of the pharmaceutical composition's active ingredients to a subject.

For example, Crumb et al. teach a pharmaceutical composition may be in form of a container (i.e. a kit is a container and the container described in Crumb is a sterile ampoule) comprising firstly of a lyophilized didemnin preparation comprised of a didemnin (i.e. aplidine and dehydrodidemnn) and a water soluble material (i.e. mannitol) and water secondly a reconstitution solution comprised of a carrier such as water used for the purpose of aiding in the injectable administration of the pharmaceutical to a subject (see, e.g. column 5 lines 66-67 and column 6 lines 12-20).

Crumb, however, does not expressly teach that the claimed active ingredient of a surfactant and/or alkanol are mixed with water within Crumb's reconstitution solution nor alkanol are mixed within a lyophilized didemnin preparation and Crumb does not expressly teach the claimed active ingredients' ranges.

Although Crumb does not expressly teach within his reference that surfactant and/or alkanol are mixed with water within Crumb's reconstitution solution, Crumb does teaches that one of ordinary skill in the art would want to utilize surfactant and/or wetting agents within its pharmaceutical formulation and/or container (see, e.g. column 6 lines 5-11). Therefore, it would have been obvious to one of ordinary skill in the art to just place the surfactant and/or wetting agents taught within Crumb's reference within Crumb's taught reconstitution solution because surfactants and/or wetting agents are well known in the art to be effective carriers to aid in the administration of an active ingredient to a subject.

Furthermore, Arai benefically teaches that the claimed alkanol (i.e. ethanol) is an effective delivery carrier to aid in the administration of an active ingredient to a subject (see, e.g. entire document including column 7 lines 9-26, tables and claims).

Moreover, Pribish benefically teaches that ethanol is also a preferred liquid carrier in injectable solutions (see, e.g. entire patent including column 6 lines 17-21).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Crumb et al.'s pharmaceutical composition and/or kit to include the active ingredient of an alkanol (i.e. ethanol) as taught by Arai and Pribish within Crumb's pharmaceutical composition and/or kit because the three combined teachings would create the claimed pharmaceutical composition and/or kit for enhanced injectable delivery of the pharmaceutical composition's active ingredients to a subject. Furthermore, the adjustment of other conventional working conditions (e.g. the substitution of one functional equivalent alkanol for another, the ranges of each active ingredient to create solubilization of the pharmaceutical composition, the substitution of one surfactant for the other and placing the reconstitution solution within a container such as a vial), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Please note that the patentability of a product does not depend upon the method of production. If the product in a product by process claim is the same as or obvious from a product of the prior art, then the claim is unpatentable even though the prior art product was made by a different process. (see, e.g. MPEP 2113).

Please note, the intended use of the above claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting (see, e.g., MPEP 2112).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Randall Winston whose telephone number is 571-272-0972. The examiner can normally be reached on 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHRISTOPHER R. TATE
PRIMARY EXAMINER